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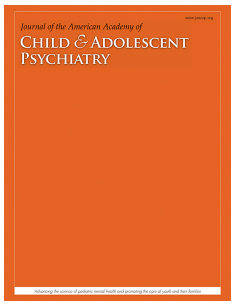

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ABSTRACT

Objective: Maternal depressive symptoms during pregnancy are associated with increased risk of psychiatric problems in children. More precise understanding of the timing of the symptoms during pregnancy and their independence from other prenatal and postnatal factors in predicting child psychopathology risk is needed. We examined whether maternal depressive symptoms during pregnancy predict child psychiatric problems, whether these associations are trimester- or gestational-week-specific and/or independent of pregnancy disorders, and whether maternal depressive symptoms after pregnancy mediate or add to the prenatal effects.

Method: The study sample comprised 2,296 women and their children born in Finland between 2006-2010, participating in the prospective pregnancy cohort study Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction (PREDO) and followed up from 1.9 to 5.9 years of age. The women completed the Center for Epidemiologic Studies Depression Scale biweekly between gestational weeks+days 12+0/13+6 and 38+0/39+6 or delivery. In the follow-up, they completed the Beck Depression Inventory-II and Child Behavior Checklist 1½-5.

Results: Maternal depressive symptoms during pregnancy predicted significantly higher internalizing (0.28 SD unit per SD unit increase [95% CI=0.24-0.32]), externalizing (0.26[0.23-0.30]) and total problems (0.31[0.27-0.35]) in children. These associations were non-specific to gestational week and hence pregnancy trimester, independent of pregnancy disorders, and independent of, though partially mediated by maternal depressive symptoms after pregnancy. Psychiatric problems were greatest in children whose mothers reported clinically significant depressive symptoms across pregnancy trimesters and during and after pregnancy.

Conclusion: Maternal depressive symptoms during pregnancy predict increased psychiatric problems in young children. Preventive interventions from early pregnancy onwards may benefit offspring mental health.

Key words: antenatal; depression; childhood mental health; psychiatric symptoms; prospective study.

INTRODUCTION

Maternal depressive symptoms affect a large proportion of pregnancies, with 7.4%-20% of women experiencing clinically significant levels of depressive symptoms at different stages of pregnancy.[1-2] These symptoms may alter the intrauterine environment, expose the fetus to unnecessarily high levels of maternal

glucocorticoids[3-5] and pro-inflammatory cytokines,[6-7] and "program" an adverse offspring phenotype, thereby explaining why maternal depressive symptoms during pregnancy predict an increased risk of psychiatric problems in the offspring.[8-19]

Yet, it still remains unclear whether maternal depressive symptoms during pregnancy are an independent risk factor for child psychiatric problems.[8-19] In the Avon Longitudinal Study of Parents and Children (ALSPAC), which is one of the two largest studies that have examined the consequences of maternal depressive symptoms during pregnancy on the offspring, maternal depressive symptoms measured at gestational weeks 18 or 32 predicted higher risks of attention problems in the offspring in early childhood,[17] and emotional and behavioral problems in pre-puberty.[12] In the Generation R study, the other of the two largest studies, maternal depressive symptoms at gestational week 20 were associated with higher risk of offspring attention problems[17] and internalizing and externalizing problems[18] in early childhood. In ALSPAC, the associations remained significant after adjusting for maternal depressive symptoms at the time of rating the child's psychiatric problems.[12,17] However, in Generation R, the associations were no longer significant,[17-18] challenging the assumption that the effects of maternal depression would be due to an adverse intrauterine environment.

While differences in sample characteristics and assessment tools may at least partially explain the contradictory findings, these and some other smaller-scale previous studies were limited to assessing maternal depressive symptoms "during the past seven days or last two weeks'' only once or twice during pregnancy.[8-19] Hence, it remains unknown whether some developmental periods during pregnancy are more vulnerable than others to the effects of maternal depressive symptoms, and if feeling depressed throughout pregnancy is more harmful for the offspring than feeling depressed only for a week or two at one or two arbitrary timepoints. However, since depressive symptoms show high stability,[8,12] disentangling gestation-week or trimester-specific effects of maternal depressive symptoms during pregnancy may prove difficult. It also remains unclear whether maternal depressive symptoms concurrent to rating the child's problems add to rather than account for, or mediate the effects of prenatal environmental adversities.

Accordingly, we examined whether depressive symptoms measured biweekly from gestational week 12 onwards up to 14 times during pregnancy in a large cohort of pregnant Finnish women predict the levels

of psychiatric problems in their 1.9–5.9-year-old children, and whether maternal depressive symptoms at the time of rating the child's problems add to, account for, or mediate any effects of maternal depressive symptoms during pregnancy. Another novel contribution of this study was to account for possible confounding by common pregnancy disorders: pre-pregnancy obesity, gestational diabetes, and hypertension-spectrum pregnancy disorders. According to previous studies, these disorders co-occur with depressive symptoms[20-21] and are associated with offspring psychiatric problems.[22-24]

METHOD

Participants

The Prediction and Prevention of Preeclampsia and Intrauterine Growth Restriction (PREDO) study enrolled 4,785 pregnant women, of whom 4,777 (8 miscarriages or stillbirths) gave birth to a singleton live-born child between 2006 and 2010.[4-5,25] The women were recruited to the study when they visited antenatal clinics at one of the ten study hospitals in Southern and Eastern Finland for their first ultrasound screening between 12+0 and 13+6 weeks+days of gestation. Of these women, 3,402 (71.2% of those with live-born offspring) filled in the biweekly depressive symptoms questionnaire during pregnancy.

In 2011-2012, 4,586 women and their children of the original sample were invited for a follow-up (three children had died after birth and before the follow-up, 33 did not have data in the Finnish nation-wide medical birth register, 55 women had declined participation in a follow-up, and for 100 women, addresses were not traceable). Of these, 2,667 women and children (58.2% of those invited) participated.

Of the 4,586 mothers invited to the follow-up, 3,279 had data on depressive symptoms during pregnancy, and 2,296 had both pregnancy and follow-up data available. The current study sample comprises these 2,296 women and their 1.9- to 5.9-year-old children (1,161 boys, 1,135 girls; 70.0% of those with data on depressive symptoms during pregnancy and invited to the follow-up).

In comparison to the non-participants in the original sample (n=2,489), the current study participants were older at delivery (mean difference=0.7 years, p<.001), had more often tertiary education (62.8% vs. 54.7%, p<.001), were less often obese (body mass index [BMI]≥30 kg/m^2) before pregnancy (12.3% vs. 15.9%, p<.001), and less often multiparous (58.1% vs. 64.4%, p<.001), smoked less often throughout pregnancy (2.8% vs. 7.1%, p<.001), and more often had a daughter (49.4% vs. 46.2%, p=.03). All

participating mothers signed informed consent forms. The PREDO study protocol was approved by ethical committees of the Helsinki and Uusimaa Hospital District.

Maternal Depressive Symptoms

The women completed the Center for Epidemiologic Studies Depression Scale (CES-D)[26] biweekly up to 14 times throughout pregnancy starting from 12+0/13+6 gestation weeks+days until 38+0/39+6 gestation weeks+days or delivery. The 20 CES-D questions were rated on a scale from none of the time (0) to all the time (3). Higher scores indicate more depressive symptoms during the past week and a sum-score of ≥16 indicates risk for clinical depression.[26-27]

In the follow-up, the women completed the Beck Depression Inventory-II (BDI-II), which comprises 21 items, each containing four statements (scored from 0 to 3) reflecting increasing severity of depressive symptoms during the past two weeks.[28] A sum-score of ≥14 indicates at least mild depressive symptomatology.[28-29]

Both depression scales have good psychometric properties,[26-31] and the CES-D has been used extensively and validated also in pregnant populations.[30-31] In our sample, the CES-D (Cronbach`s α=.88 to .92 in the 14 biweekly measurement points) and the BDI-II (α=.91) showed high internal consistency.

Child Psychiatric Problems

Child Behavior Checklist for ages 1½-5 (CBCL/1½-5), filled in by the child`s mother, comprises 99 problem items rated on a scale of not true (0) to very true or often true (2).[32] The CBCL/1½-5 yields scores for three main scales (internalizing, externalizing, and total problems), seven syndrome scales (emotionally reactive, anxious/depressed, somatic complaints, withdrawn, sleep problems, attention problems, and aggressive behavior) and five *DSM*-oriented scales (affective, anxiety, pervasive developmental, attention deficit/hyperactivity, and oppositional defiant problems).[34] A t-score of ≥60 on the main and of ≥65 on the syndrome and *DSM*-oriented scales indicates at least borderline clinically significant problems.[32] The CBCL/1½-5 has good test-retest reliability, internal consistency, and criterion validity.[32-33]

Pregnancy Disorders

Data on maternal pregnancy disorders were extracted from medical reports independently verified by a clinical jury and/or from the Finnish Medical Birth Register.[25] These included pre-pregnancy obesity

(BMI≥30 kg/m^2 vs. BMI<30 kg/m^2), hypertension spectrum pregnancy disorders (preeclampsia, gestational hypertension; yes/no), and gestational diabetes (yes/no).[21,25,34-35]

Covariates

These included maternal age at delivery (years), smoking during pregnancy (did not smoke/quit during first trimester/smoked throughout pregnancy), parity (primiparous/multiparous) chronic hypertension (yes/no), type 1 diabetes (yes/no), child's sex, gestational length (weeks), birth weight (g), and family structure at childbirth (cohabitation/marriage vs. single parent), with data extracted from medical reports and/or Medical Birth Register; maternal history of physician-diagnosed depression before pregnancy (yes/no), psychotropic medication use during pregnancy (antidepressants, other [barbiturates, sedatives, antipsychotics] vs. no), alcohol use during pregnancy (yes/no), and education level (basic/secondary vs. tertiary), each self-reported in a questionnaire given to the mothers at 12+0-13+6 weeks+days of gestation; and child's age at follow-up (years), which was reported in conjunction with filling in the CBCL questionnaire.

Data Analysis

We examined the course of depressive symptoms during pregnancy with latent profile analysis and Pearson correlation analysis.

Next, we inspected the crude unadjusted mean differences of maternal depressive symptoms across the 14 measurement points during pregnancy according to child internalizing, externalizing, and total problems scores above and below the borderline clinical cutoff, and calculated Cohen's d's for effect sizes.

We then used linear regression analyses to test associations between maternal depressive symptoms during pregnancy and child internalizing, externalizing, and total problems. We examined gestation week-specific effects and also calculated a trimester-weighted mean value of depressive symptoms across pregnancy (mean of the only value from first pregnancy trimester and the mean values of second trimester and third trimester) and square-root transformed the values to normalize the distributions. Since scores in the CBCL/1½-5 syndrome and *DSM*-oriented scales below 50 were truncated into 50 according to the manual,[32] resulting in strongly skewed distributions and a "floor effect," Tobit regressions were used in the analyses of these scales. To facilitate interpretation, both the predictor and outcome variables were standardized to the

mean of 0 and SD of 1.

The associations of maternal depressive symptoms during pregnancy with child psychiatric problems were examined in four different linear or Tobit regression models. Model 1 was adjusted for child's age and sex. Model 2 was adjusted for the covariates in model 1 and family structure, maternal age at childbirth, parity, education level, type 1 diabetes, chronic hypertension, history of depression before pregnancy, antidepressant and other psychotrophic medication use, alcohol use and smoking during pregnancy, gestation length, and infant's birth weight adjusted for sex and gestation length. Model 3 was adjusted for the model 2 covariates and prepregnancy obesity, gestational diabetes, and hypertension-spectrum pregnancy disorders. Model 4 was adjusted for the model 3 covariates and maternal depressive symptoms after pregnancy at the time of rating the child's psychiatric problems.

With linear and/or Tobit regressions, we also tested whether child psychiatric problem scores increased according to the number of pregnancy trimesters (0,1,2,3) during which the mean maternal CES-D score was above the clinical cut-off of $\geq$16; whether child psychiatric problem scores differed between the groups of mothers identified by a latent profile analysis based on their depressive symptoms scores across pregnancy; whether maternal pregnancy disorders accounted for the effects of maternal depressive symptoms during pregnancy (analyses were adjusted for the pregnancy disorders and re-run separately in mothers with and without pregnancy disorders); and whether maternal depressive symptoms after pregnancy accounted for (postpartum depressive symptoms were added as a covariate into the 4th regression models), mediated (mediation analyses were performed with the bootstrapping method using 5000 bootstrapping re-samples with bias-corrected confidence intervals), or added to the effects of maternal depressive symptoms during pregnancy (interaction term of depressive symptoms during pregnancy x after pregnancy was entered into the regression equation followed by the main effects).

In additional analyses, we studied age-specific associations by re-running the analyses separately among children who were 1.9-3.9 years and 4.0-5.9 years at follow-up. We also re-ran the analyses separately among children born to mothers with and without depression diagnoses before pregnancy. Finally, in a subsample from whom we had paternal CES-D depressive symptoms data available when the children were 6 months old (n=1,237), we examined if paternal depressive symptoms confounded any

effects of maternal depressive symptoms.

RESULTS

Table 1 shows the characteristics of the study sample. The CES-D scores were highly intercorrelated across pregnancy (Pearson r`s between .44 and .80, p-values<.001). Latent profile analysis identified a solution with three groups as the most optimal (in comparison to solutions with fewer and larger number of groups) to depict depressive symptoms throughout pregnancy (Akaike Information Criterion = 184565.50, sample-size-adjusted Bayesian Information Criterion=184714.10, Vuong-Lo-Mendell-Rubin LRT and Lo-Mendell-Rubin Adjusted Likelihood Ratio Test p-values =.02). In all three groups, which differed from each other in their level of depressive symptoms, depressive symptoms showed high stability. One trajectory was described by consistently high, one by consistently moderate, and one by consistently low depressive symptom scores (Figure S1, available online). The CES-D mean score during pregnancy also correlated significantly with the BDI-II score in the follow-up (r=.45, p<.001), and child internalizing, externalizing, and total problems were highly inter-correlated (r`s from .62 to .90, p-values<.001). Maternal pregnancy disorders were not associated with child psychiatric problems, but maternal history of depression before pregnancy was associated with significantly higher child internalizing, externalizing, and total psychiatric problems. Table S1 (available online) shows these and the associations of the other covariates with child psychiatric problems.

Maternal Depressive Symptoms During Pregnancy and Child Psychiatric Problems

Figure 1 (Panel A) shows that at each biweekly measurement point during pregnancy, mothers whose children scored above the borderline clinical cutoffs in internalizing, externalizing, and total problems had significantly higher depressive symptom scores than mothers whose children scored below the cutoffs; these group differences were of medium effect size (Cohen's d's varying from 0.36 to 0.52).

Figure 1 (Panel B) and Tables S2, S3 (available online) show that the effects of maternal depressive symptoms across pregnancy and at each biweekly assessment on child internalizing, externalizing, and total problems were significant when adjusted for covariates in linear regression models 1-2. Table S2 (available online) shows that higher maternal mean depressive symptoms during pregnancy also predicted significantly higher CBCL syndrome- and *DSM*-oriented problem scores of the child across Tobit regression models 1-2.

As shown in Figure 2 (Panel A), child internalizing, externalizing, and total psychiatric problem scores increased linearly according to the number of pregnancy trimesters during which the mother reported mean depressive symptoms above the clinical cutoff of ≥16. We also compared the psychiatric problems of children of mothers with consistently high, moderate, and low depressive symptoms during pregnancy, as identified by the latent profile analysis. Figure 2 (Panel B) shows that child internalizing, externalizing, and total psychiatric problem scores were the highest in children born to mothers who had consistently high depressive symptoms during pregnancy. Adjustments for covariates in models 1-4 had no effects on these associations (Figure 2).

Pregnancy Disorders, Maternal Depressive Symptoms During Pregnancy and Child Psychiatric Problems

When we made further adjustments for maternal pre-pregnancy obesity, hypertension-spectrum pregnancy disorders, and gestational diabetes, all the associations between maternal depressive symptoms during pregnancy and child psychiatric problems remained significant (Figures 1 [Panel B, model 3] and 2 and Tables S2-S3, model 3, available online). We re-ran the analyses in groups who were and were not exposed to maternal pregnancy disorders, and in both groups, the associations were significant (Figure S2, available online).

The Moderating and Partially Mediating Effects of Maternal Depressive Symptoms After Pregnancy

Figures 1 (Panel B, model 4) and 2 and Tables S2-S3 (model 4, available online) show that, although maternal depressive symptoms after pregnancy, concurrently to rating the child psychiatric problems, were significantly associated with higher internalizing, externalizing, and total problems as well as syndrome scale- and *DSM*-oriented problems of the child (unstandardized regression coefficients in 4th regression models =0.22 to 0.47, p-values<.001), maternal depressive symptoms across pregnancy and at each biweekly assessment remained significant predictors of all types of child psychiatric problems after adjustment for maternal depressive symptoms after pregnancy; although in effect size these associations were somewhat attenuated. Mediation analyses demonstrated that while maternal depressive symptoms during pregnancy had a direct effect on child internalizing, externalizing, and total problems, maternal depressive symptoms after pregnancy partially mediated the prenatal effects (Figure 3).

In addition to partially mediating the prenatal effects, maternal depressive symptoms after pregnancy added to the effects of depressive symptoms during pregnancy on internalizing (p-value for interaction between maternal depressive symptoms during x after pregnancy=.02) and total problems (p for interaction=.049). Figure 4 shows that child internalizing and total problems scores were greatest if the mother reported both prenatal depressive symptoms above the clinical cutoff of ≥16 and depressive symptoms after pregnancy above the clinical cutoff of ≥14, compared to the scores of children whose mothers had clinically significant symptomatology either during or after pregnancy or who had both scores below the clinical cutoffs.

The Age-Specificity of the Effects of Maternal Depressive Symptoms During Pregnancy and the Moderating Role by Maternal History of Depression Before Pregnancy

Table S4 (available online) shows that higher maternal depressive symptoms during pregnancy independently predicted significantly higher child internalizing, externalizing, and total problems both among children who were 1.9-3.9 and 4.0-5.9 years old.

Higher maternal depressive symptoms during pregnancy predicted higher psychiatric problems both among children born to mothers with and without a diagnosis of depression before pregnancy (Figure S3, available online). However, the associations with internalizing problems were inconsistent across models 1-4 among children whose mothers had been diagnosed with depression before pregnancy.

No Confounding by Paternal Depressive Symptoms in Child's Infancy

At child age 6 months, 1,237 fathers assessed their depressive symptoms (mean=7.4, SD=6.0: r=.15 and r=.11 with maternal depressive symptoms during and after pregnancy, respectively, p-values<.001). Linear regression analyses in this subsample showed that maternal depressive symptoms during pregnancy predicted significantly higher child internalizing, externalizing, and total problems independently of model 4 covariates and paternal depressive symptoms (unstandardized regression coefficients=0.17, =0.15, and =0.19, respectively, p-values<.001).

DISCUSSION

Our prospective study shows that higher maternal depressive symptoms during pregnancy predicted significantly higher levels of child psychiatric problems in early childhood across all the domains captured

by the CBCL.[32] While maternal depressive symptoms after pregnancy at the time of evaluating the child's psychiatric problems were also associated with significantly higher child psychiatric problems, the prenatal effects were not accounted for by the after-pregnancy effects. Instead, higher maternal depressive symptoms after pregnancy only partially mediated the prenatal effects. Additional analyses showed that they also added to child psychiatric problems, such that children of mothers with clinically significant depressive symptoms both during and after pregnancy had the highest internalizing and total problems scores. All the associations were independent of a number of important covariates, including common pregnancy disorders and paternal depressive symptoms when the children were 6 months old.

That the effects of maternal depressive symptoms during pregnancy on child psychiatric problems were independent of depressive symptoms after pregnancy correspond well with findings from ALSPAC[12,17] but contradict findings from Generation R,[17-18] studies of comparable sample size to ours. In ethnic background, our sample is more similar to the ALSPAC, which comprises almost entirely Caucasian offspring, than it is to the multiethnic Generation R. This offers one possible explanation why our findings differ from the findings in Generation R. Most importantly, however, our study captured depressive symptomatology throughout the entire pregnancy unprecedented by these two and any other previous studies.[8-19] The multiple, repeated, biweekly measurements in our study indeed reduced measurement error and increased the reliability and internal validity of our findings. Hence, our study offers the most comprehensive view reported so far on the effects of maternal depressive symptoms during pregnancy on child psychiatric problems.

The repeated measurements allowed us also to capture any gestational-week-specific effects. This is relevant since maternal physiology changes during pregnancy and pregnant women become physiologically more stress resistant as pregnancy advances.[36] Yet, we found that maternal depressive symptoms showed high stability across the biweekly measurements. Therefore, it was not surprising to discover that the effects of depressive symptoms on child psychiatric problems were non-specific to gestation week and hence pregnancy trimester. Regardless of detecting these non-specific effects, the level of child psychiatric problems increased according to the number of pregnancy trimesters during which the mother reported clinically significant depressive symptoms. This highlights the importance of evaluating depressive

symptoms multiple times during pregnancy. An alternative explanation for these findings is that they reflect both the chronicity and the severity of depressive symptoms throughout pregnancy. While our study does not provide the means to disentangle chronicity from severity, the results of our latent profile analysis showing that child psychiatric problems were the highest in the group of mothers who had consistently high depressive symptoms during pregnancy favors this interpretation.

Although the effects of maternal depressive symptoms during pregnancy were clearly independent of symptoms reported after pregnancy, maternal depressive symptoms after pregnancy still played a role in two important ways: symptoms after pregnancy both partially mediated and added to the prenatal effects. These findings emphasize that both the pre- and the postnatal periods should be targets of preventive interventions and reinforce the assessment of maternal depressive symptoms in routine antenatal and postpartum health care.[2]

The effects of maternal depressive symptoms during pregnancy on child psychiatric problems were also independent of maternal physician-diagnosed depression before pregnancy, although the effects were more pronounced and evident on all types of child psychiatric problems in the group who did not report physician-diagnosed depression before pregnancy. Among those with history of depression, intrauterine effects did not systematically add to the effects on internalizing symptoms but did predict externalizing and total problems. These somewhat contrasting findings may well reflect the much larger group of mothers with no physician-diagnosed depression before pregnancy available for analysis in our study.

Fetal overexposure to maternal glucocorticoids and inflammatory cytokines may underlie the prenatal programming effects. For instance, previous studies have demonstrated that higher maternal depressive symptoms during pregnancy are associated with higher mRNA levels of the glucocorticoid receptor (GR) and mineralocorticoid receptor genes in the placenta[4] and that higher placental GR mediate the effects of maternal depressive symptoms on infant regulatory behavior.[5] Other studies have pointed to associations of maternal depression during pregnancy with epigenetic modifications of the GR gene in the placenta and fetal cord blood DNA[3] and found cross-sectional associations between altered GR gene methylation in DNA from peripheral blood leukocytes with adolescent internalizing problems.[37] Also, higher maternal prenatal pro-inflammatory marker levels have been associated with both maternal depressive

symptoms during pregnancy[6-7] and offspring autism risk.[38] However, the sociobiological pathways underlying the development of maternal depression and child psychopathology are beyond the scope of this study. Further studies unraveling these underlying mechanisms and studies focusing on the underlying genetic and epigenetic mechanisms are warranted.

Strengths of our study include a sizable, homogenous sample, prospective design, repeated measurements of depressive symptoms during pregnancy and concurrently when rating child's psychiatric problems, and data on multiple important covariates. The homogeneity of the sample is, however, also a limitation, as is the follow-up sample attrition that was not independent of maternal characteristics. Half of the original cohort was lost to follow-up, which limits the external validity of our findings. Furthermore, we had a single informant on child problems. Using multiple informants would have given a more comprehensive picture of the associations. However, maternal depressive symptoms during pregnancy have previously been shown to predict child psychiatric problems, whether these were assessed by parents, teachers, self-reports, or clinical interviews.[8-19] Another limitation is that we only had data on paternal depressive symptoms for a subsample. Furthermore, while we had data on paternal depressive symptoms when the child was 6 months old, we did not have paternal depressive symptoms available when the mother was pregnant. Although adjustment for paternal depressive symptoms at 6 months did not influence our findings, further studies are needed to clarify the contribution of paternal depressive symptoms to maternal intrauterine effects. While paternal depression is an important covariate implicating familial confounding, adjustment for paternal depressive symptoms did not influence our findings. Although we made adjustments for family structure, we lacked data on relationship stress that may contribute to the association between maternal depression and child psychopathology.[8] Moreover, generalizations from our findings cannot be made to psychiatric disorders since we measured psychiatric problems dimensionally. Since the mothers rated their depressive symptoms after pregnancy concurrently to child problems, shared method variance may have inflated the effect size estimates of the associations found, as mothers with depression may perceive more problems in their children. Also the mediation effects observed do not, strictly defined, evidence mediation, since child well-being may also influence maternal mental state. However, reverse causation cannot explain the prenatal effects.

In conclusion, our prospective study showed that higher maternal depressive symptoms during pregnancy predict significantly higher psychiatric problems in children. These associations were non-specific to pregnancy trimester and gestational week and independent of, though partially mediated by, maternal depressive symptoms after pregnancy. Psychiatric problem levels were greatest in children whose mothers reported clinically significant depressive symptoms across pregnancy trimesters and both during and after pregnancy. Ongoing studies will unravel the biological and psychosocial mechanisms and enable the design of preventive, targeted, family-based interventions, which, according to our findings, should focus both on the mother and her baby and start from early pregnancy onwards.

Clinical Guidance

●Our findings show that maternal depressive symptoms should be assessed as a part of routine antenatal and postpartum care due to their adverse consequences for both the mothers and their children.

●Maternal depressive symptoms during pregnancy predict increased psychiatric problems in children independently of cardiometabolic pregnancy disorders and maternal depressive symptoms postpartum.

●Maternal depressive symptoms show high stability throughout pregnancy and remain stable from pregnancy to postpartum and have additive effects on child psychiatric problems.

●Early interventions may prevent psychiatric problems both in the mother and the child.

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Table 1. Characteristics of the Sample

	Data Available(N)	Mean(SD)/N(%)
Maternal characteristics		
Age at delivery (years)	2296	31.9 (4.6)
Education, tertiary	2296	1443 (62.8 %)
Parity, primiparous	2291	961 (41.9 %)
Family structure, single	2193	35 (1.6 %)
Pre-pregnancy BMI (kg/m^2)	2296	24.3 (4.8)
Obese (BMI≥30)		283 (12.3 %)
History of depression before pregnancy, Yes	2186	214 (9.8%)
Antidepressants medication use during pregnancy, Yes	1952	49 (2.5 %)
Other psychotropic medication use during pregnancy, Yes	1952	14 (0.7 %)
Gestational hypertension-spectrum disorder, Yes	2296	179 (7.8 %)
Chronic hypertension, Yes	2296	83 (3.6 %)
Gestational diabetes, Yes	2296	235 (10.2 %)
Type 1 diabetes, Yes	2296	11 (0.5 %)
Alcohol use during pregnancy, Yes	2275	374 (16.4 %)
Smoking during pregnancy, No	2296	2156 (93.9 %)
Quit during the first trimester		75 (3.3 %)
Smoked throughout pregnancy		65 (2.8 %)
Depressive symptoms during pregnancy		
Trimester-weighted mean of center for epidemiologic studies depression Scale sum-scores	2296	11.4 (6.4)
Trimester-weighted mean of center for epidemiologic studies depression Scale sum-scores≥16	2296	489 (21.3 %)
Depressive symptoms after pregnancy		
BDI-II sum-score	2269	6.4 (6.3)
BDI-II sum-score≥14, yes	2269	274 (12.1 %)
Child characteristics		
Sex, boys	2296	1161 (50.6 %)
Gestational age (weeks)	2296	39.9 (1.6)
Birth weight (grams)	2296	3520.9 (510.9)
Age at follow-up (year)	2296	3.5 (0.7)
Child Behavior Checklist/1½-5 Psychiatric Problems		
Main scales		
Internalizing problems	2296	45.8 (9.4)
Scored above the borderline clinical cutoff, Yes	2296	197 (8.6 %)
Externalizing problems	2296	47.5 (9.1)
Scored above the borderline clinical cutoff, Yes	2296	225 (9.8 %)
Total problems	2296	46.4 (9.2)
Scored above the borderline clinical cutoff, Yes	2296	183 (8.0 %)
Syndrome scales		
Emotionally reactive	2296	52.9 (4.8)
Anxious/depressed	2296	51.1 (2.9)
Somatic complaints	2296	54.0 (5.9)
Withdrawn	2296	53.0 (4.5)
Sleep problems	2296	54.1 (5.5)
Attention problems	2296	51.9 (3.5)
Aggressive behaviour	2296	53.1 (5.2)
DSM-oriented scales		
Affective problems	2296	53.6 (5.0)
Anxiety problems	2296	52.1 (4.2)
Pervasive developmental problems	2296	53.3 (5.3)
ADHD problems	2296	52.1 (3.8)
Oppositional defiant problems	2296	53.7 (5.5)

Note: ADHD = attention-deficit/hyperactivity disorder; BDI = Beck Depression Inventory; BMI = body mass index; ODD = oppositional defiant disorder.

FIGURE TITLES AND LEGENDS

Figure 1. Maternal depressive symptoms during pregnancy and psychiatric problems in children. Note: Panel A: Crude unadjusted means and 95% CIs (error bars) of maternal biweekly depressive symptoms during pregnancy according to child's Internalizing, Externalizing, and Total Problems scores above (solid lines) and below (dashed lines) the borderline clinical cutoffs. Panel B: Unstandardized regression coefficients (B) and 95% CIs of linear regression analyses on the associations between trimester-weighted mean of maternal depressive symptoms during pregnancy and child internalizing, externalizing, and total problems in linear regression models 1-4. SD = standard deviation.

Figure 2. Additive effects of maternal trimester-specific depressive symptoms during pregnancy on child psychiatric problems. Note: Panel A: Estimated marginal means and 95% CIs of child internalizing, externalizing, and total problems according to the number of pregnancy trimesters during which the mother had mean depressive symptoms above the clinical cutoff of ≥16 are shown. Estimated marginal means are adjusted for child's age and sex; p-values refer to linear trends in regression models 1-4. Panel B: Estimated marginal means and 95% CIs of child internalizing, externalizing, and total problems in three groups identified by latent profile analysis on maternal depressive symptoms across pregnancy. Estimated marginal means are adjusted for child's age and sex; p values refer to linear trends in regression models 1-4.

Figure 3. Maternal depressive symptoms during pregnancy partially act via symptoms after pregnancy on child psychiatric problems. Note: Mediation analyses showing that maternal depressive symptoms during pregnancy partially act via maternal depressive symptoms after pregnancy to impact on child internalizing (Panel A), externalizing (Panel B), and total (Panel C) problems are shown. The numbers represent unstandardized regression coefficients (B), 95% CIs, and p values. The estimates are adjusted for child's age and sex; p values refer to effects in regression models 1-3.

Figure 4. Additive effects of maternal depressive symptoms during and after pregnancy on child internalizing and total problems. Note: Estimated marginal means and 95% CIs of child internalizing (Panel A) and total (Panel B) problems according to mean maternal depressive symptoms during pregnancy above and below the clinical cutoff of ≥16 on the Center for Epidemiologic Studies Depression Scale (CES-D) and after pregnancy above and below the clinical cutoff of ≥14 on the Beck Depression Inventory-II (BDI-II) are shown. The estimated marginal means are adjusted for child's age and sex: p values refer to linear trends in regression models 1-3.

Figure S1. Latent profile analysis on the course of maternal depressive symptoms during pregnancy. Note: The figure shows the mean levels of depressive symptoms at different gestational weeks in three latent profile analysis-derived groups of mothers who show consistently low, moderate, and high levels of depressive symptoms throughout pregnancy. CES-D = Center for Epidemiologic Studies Depression Scale.

Figure S2. Maternal depressive symptoms during pregnancy and child psychiatric problems in groups with and without pregnancy disorders. Note: Maternal depressive symptoms during pregnancy and child psychiatric problems among those with maternal pregnancy disorders (pre-pregnancy obesity, gestational hypertensive disorders, and gestational diabetes) (Panel A: n=541) and among those without (Panel B: n=1,755) are shown. Unstandardized regression coefficients (B) and their 95% CI of linear regression models adjusted for the covariates in models 1-3. The third models refer here to

regression models adjusted further for maternal depressive symptoms at the time of rating the child's problems.

Figure S3. Maternal depressive symptoms during pregnancy and child psychiatric problems in groups with and without maternal diagnosis of depression before pregnancy. Note: Maternal depressive symptoms during pregnancy and child psychiatric problems among those with maternal self-reported history of physician-diagnosed depression before pregnancy (Panel A: n=214) and among those without (Panel B: n=1,982) are shown. Unstandardized regression coefficients (B) and their 95% CI of linear regression models adjusted for the covariates in models 1-4.

Table S1. The Associations of the Covariates With Child Psychiatric Problems

	CBCL Scale					
	Internalizing Problems[a]		**Externalizing Problems[a]**		**Total Problems[a]**	
Maternal Characteristics	**r /Mean Difference[b]**	**p**	**r /Mean Difference[b]**	**p**	**r /Mean Difference[b]**	**p**
Age at delivery	-.09	<.001	-.11	<.001	-.12	<.001
Education: Primary or secondary vs. tertiary	.05	.31	.11	.01	.08	.05
Parity: Primiparous vs. other	.40	<.001	.21	<.001	.34	<.001
Family structure: single vs. cohabiting	.17	.30	.04	.83	.08	.63
History of depression before pregnancy (yes vs. no)	.24	.002	.20	.01	.26	<.001
Antidepressant use during pregnancy (yes vs. no)	.02	.88	.26	.07	.21	.14
Other psychotropic medication use during pregnancy (yes vs. no)	.37	.17	.43	.11	.44	.10
Alcohol Use During Pregnancy (yes vs. no)	.01	.91	.06	.29	.01	.83
Quit smoking during first trimester vs. no smoking during pregnancy	.18	.13	.23	.04	.22	.06
Smoked throughout pregnancy vs. no smoking during pregnancy	.31	.01	.49	<.001	.44	.001
Smoked throughout pregnancy vs. quit during first trimester	.13	.43	.25	.13	.21	.20
Pre-pregnancy obesity (yes/no)	-.03	.63	.09	.18	.04	.56
Gestational hypertension-spectrum disorder (yes/no)	-.00	.95	-.00	.96	-.00	.99
Chronic hypertension (yes/no)	-.00	>.99	-.08	.50	-.04	.74
Gestational diabetes (yes/no)	-.02	.80	-.02	.76	-.01	.87
Type 1 Diabetes (yes/no)	.17	.56	.39	.20	.27	.37
Child Characteristics						
Sex (Boy vs. Girl)	-.03	.48	.26	<.001	.15	<.001
Gestational age	-.03	.13	-.03	.21	-.03	.16
Birth weight adjusted for gestational age and sex	-.08	<.001	-.05	.03	-.06	.005
Age at follow-up	.07	.002	-.08	<.001	-.04	.03
Paternal depressive symptoms in child's infancy	.14	<.001	.08	.003	.14	<.001

Note: CBCL = Child Behavior Checklist.

[a] Child psychiatric problem scores are expressed in standard deviation units

[b] r refers to Pearson correlation coefficients of continuous covariates with child psychiatric problems; mean difference refers to mean group differences between the groups of the categorical covariates in child psychiatric problems in independent samples t-test analyses.

Table S2. The Associations Between Trimester-Weighted Mean of Maternal Depressive Symptoms During Pregnancy and Child Psychiatric Problems

CBCL Scale	**Model 1 (n=2,296)[a]**		**Model 2 (n=2,296)[a]**		**Model 3 (n=2,296)[a]**		**Model 4(n=2,269)[a,b]**	
Main Scales	**B(95% CI)[c]**	**p**	**B(95% CI)[c]**	**p**	**B(95% CI)[c]**	**p**	**B(95% CI)[c]**	**p**
Internalizing Problems	0.28(0.24-0.32)	<.001	0.28(0.24-0.32)	<.001	0.29(0.25-0.33)	<.001	0.18(0.13-0.22)	<.001
Externalizing Problems	0.26(0.23-0.30)	<.001	0.26(0.22-0.30)	<.001	0.26(0.22-0.30)	<.001	0.16(0.12-0.20)	<.001
Total Problems	0.31(0.27-0.35)	<.001	0.31(0.27-0.35)	<.001	0.31(0.27-0.35)	<.001	0.20(0.15-0.24)	<.001
Syndrome Scales								
Emotionally Reactive	0.41(0.33-0.49)	<.001	0.41(0.33-0.48)	<.001	0.42(0.34-0.49)	<.001	0.25(0.17-0.34)	<.001
Anxious/Depressed	0.56(0.44-0.68)	<.001	0.56(0.44-0.68)	<.001	0.56(0.44-0.68)	<.001	0.35(0.23-0.48)	<.001
Somatic Complaints	0.37(0.29-0.45)	<.001	0.38(0.30-0.47)	<.001	0.39(0.30-0.47)	<.001	0.26(0.17-0.35)	<.001
Withdrawn	0.29(0.23-0.36)	<.001	0.33(0.26-0.39)	<.001	0.33(0.26-0.39)	<.001	0.20(0.13-0.27)	<.001
Sleep Problems	0.30(0.24-0.36)	<.001	0.30(0.24-0.36)	<.001	0.30(0.24-0.36)	<.001	0.20(0.13-0.27)	<.001
Attention Problems	0.35(0.28-0.43)	<.001	0.35(0.28-0.43)	<.001	0.35(0.27-0.43)	<.001	0.22(0.13-0.30)	<.001
Aggressive Behaviour	0.46(0.38-0.54)	<.001	0.45(0.37-0.53)	<.001	0.45(0.37-0.53)	<.001	0.28(0.19-0.37)	<.001
***DSM*-Oriented Scales**								
Affective Problems	0.30(0.25-0.35)	<.001	0.30(0.25-0.36)	<.001	0.31(0.25-0.36)	<.001	0.20(0.14-0.25)	<.001
Anxiety Problems	0.45(0.36-0.55)	<.001	0.44(0.34-0.54)	<.001	0.44(0.34-0.54)	<.001	0.29(0.19-0.40)	<.001
Pervasive Developmental Problems	0.32(0.26-0.39)	<.001	0.34(0.27-0.41)	<.001	0.34(0.28-0.41)	<.001	0.21(0.14-0.29)	<.001
ADHD Problems	0.39(0.31-0.47)	<.001	0.40(0.32-0.48)	<.001	0.40(0.32-0.48)	<.001	0.25(0.16-0.33)	<.001
Oppositional Defiant Problems	0.31(0.25-0.37)	<.001	0.31(0.24-0.37)	<.001	0.31(0.25-0.37)	<.001	0.18(0.12-0.25)	<.001

Note: ADHD = attention-deficit/hyperactivity disorder; CBCL = Child Behavior Checklist.

[a] Model 1 is adjusted for the age and sex of the child; Model 2 further for family structure, maternal age at delivery, parity, education level, type 1 diabetes, chronic hypertension, history of depression before pregnancy, antidepressant and other psychotropic medication use, alcohol use and smoking during pregnancy, gestation length and child's birth weight adjusted for gestation length and sex; Model 3 further for pre-pregnancy obesity, hypertension-spectrum pregnancy disorders and gestational diabetes: and Model 4 for maternal depressive symptoms after pregnancy at the time of rating the child's psychiatric problems.

[b] The fourth analytic model includes 2269 participants since 27 mothers had missing data on depressive symptoms after pregnancy and were excluded from these analyses. In contrast, participants with missing values on categorical covariates were dummy-coded into separate categories in the regression analysis.

[c] Bs and 95% CIs for main scales are unstandardized regression coefficients and their 95% CIs are from linear regression analyses: Bs and 95% CIs for syndrome and *DSM*-Oriented Scales are unstandardized regression coefficients and 95 % confidence intervals from tobit regression analyses. Both the independent and dependent variables are expressed in standard deviation units.

Table S3. Maternal Biweekly Depressive Symptoms During Pregnancy and Child Psychiatric Problems

Maternal Depressive Symptoms at	**Internalizing Problems**	**Externalizing Problems**	**Total Problems**
12-13 weeks of gestation (n=2193)	B (95% CI)	B (95% CI)	B (95% CI)
Model 1	0.22 (0.17-0.26)	0.22 (0.18-0.27)	0.25 (0.21-0.29)
Model 2	0.22 (0.18-0.26)	0.22 (0.18-0.26)	0.25 (0.21-0.29)
Model 3	0.22 (0.18-0.26)	0.22 (0.18-0.26)	0.25 (0.21-0.29)
Model 4	0.12 (0.07-0.16)	0.13 (0.08-0.17)	0.14 (0.10-0.18)
14-15 weeks of gestation (n=2142)			
Model 1	0.22 (0.18-0.26)	0.22 (0.17-0.26)	0.25 (0.21-0.29)
Model 2	0.24 (0.19-0.28)	0.21 (0.16-0.25)	0.25 (0.21-0.29)
Model 3	0.22 (0.18-0.26)	0.20 (0.16-0.25)	0.25 (0.21-0.29)
Model 4	0.12 (0.08-0.17)	0.12 (0.07-0.16)	0.14 (0.10-0.18)
16-17 weeks of gestation (n=2110)			
Model 1	0.23 (0.19-0.27)	0.21 (0.17-0.25)	0.26 (0.21-0.30)
Model 2	0.23 (0.19-0.28)	0.21 (0.17-0.25)	0.25 (0.21-0.29)
Model 3	0.24 (0.20-0.28)	0.21 (0.16-0.25)	0.25 (0.21-0.29)
Model 4	0.14 (0.10-0.18)	0.12 (0.08-0.16)	0.15 (0.11-0.19)
18-19 weeks of gestation (n=2133)			
Model 1	0.21 (0.17-0.25)	0.20 (0.16-0.24)	0.24 (0.20-0.28)
Model 2	0.20 (0.16-0.24)	0.19 (0.15-0.23)	0.23 (0.19-0.27)
Model 3	0.20 (0.16-0.25)	0.19 (0.15-0.23)	0.23 (0.19-0.27)
Model 4	0.12 (0.07-0.16)	0.11 (0.07-0.15)	0.13 (0.09-0.17)
20-21 weeks of gestation (n=2111)			
Model 1	0.23 (0.19-0.27)	0.22 (0.17-0.26)	0.25 (0.21-0.30)
Model 2	0.23 (0.19-0.27)	0.21 (0.16-0.25)	0.25 (0.21-0.29)
Model 3	0.23 (0.19-0.27)	0.20 (0.16-0.25)	0.25 (0.21-0.29)
Model 4	0.13 (0.09-0.18)	0.12 (0.07-0.16)	0.15 (0.11-0.19)
22-23 weeks of gestation (n=2081)			
Model 1	0.22 (0.17-0.26)	0.22 (0.18-0.26)	0.25 (0.20-0.29)
Model 2	0.21 (0.17-0.25)	0.21 (0.17-0.25)	0.24 (0.20-0.28)
Model 3	0.21 (0.17-0.26)	0.21 (0.16-0.25)	0.24 (0.20-0.28)
Model 4	0.12 (0.07-0.16)	0.12 (0.08-0.16)	0.14 (0.09-0.18)
24-25 weeks of gestation (n=2055)			
Model 1	0.23 (0.19-0.27)	0.21 (0.17-0.25)	0.25 (0.20-0.29)
Model 2	0.22 (0.18-0.26)	0.20 (0.15-0.24)	0.23 (0.19-0.27)
Model 3	0.22 (0.18-0.27)	0.19 (0.15-0.24)	0.23 (0.19-0.28)
Model 4	0.13 (0.09-0.18)	0.11 (0.07-0.16)	0.14 (0.09-0.18)
26-27 weeks of gestation (n=2076)			
Model 1	0.23 (0.18-0.27)	0.22 (0.18-0.26)	0.25 (0.21-0.29)
Model 2	0.22 (0.18-0.26)	0.21 (0.17-0.25)	0.24 (0.20-0.28)
Model 3	0.22 (0.18-0.26)	0.21 (0.17-0.25)	0.24 (0.20-0.28)
Model 4	0.12 (0.08-0.17)	0.12 (0.08-0.17)	0.14 (0.10-0.18)
28-29 weeks of gestation (n=2055)			
Model 1	0.26 (0.22-0.30)	0.22 (0.18-0.26)	0.27 (0.23-0.31)
Model 2	0.26 (0.21-0.30)	0.21 (0.17-0.25)	0.26 (0.22-0.31)
Model 3	0.26 (0.22-0.30)	0.21 (0.17-0.25)	0.26 (0.22-0.31)
Model 4	0.16 (0.12-0.21)	0.12 (0.08-0.16)	0.16 (0.12-0.20)
30-31 weeks of gestation (n=2056)			
Model 1	0.25 (0.20-0.29)	0.22 (0.18-0.26)	0.27 (0.23-0.31)
Model 2	0.25 (0.21-0.29)	0.22 (0.18-0.26)	0.27 (0.23-0.31)

Model 3	0.25 (0.21-0.30)	0.22 (0.18-0.26)	0.27 (0.23-0.31)
Model 4	0.16 (0.11-0.20)	0.13 (0.08-0.17)	0.16 (0.12-0.21)
32-33 weeks of gestation (n=2061)			
Model 1	0.26 (0.22-0.30)	0.23 (0.19-0.27)	0.28 (0.24-0.32)
Model 2	0.27 (0.23-0.31)	0.23 (0.19-0.27)	0.28 (0.24-0.32)
Model 3	0.27 (0.23-0.31)	0.23 (0.19-0.27)	0.28 (0.24-0.32)
Model 4	0.18 (0.13-0.22)	0.14 (0.09-0.18)	0.18 (0.13-0.22)
34-35 weeks of gestation (n=2020)			
Model 1	0.25 (0.20-0.29)	0.22 (0.18-0.26)	0.27 (0.22-0.31)
Model 2	0.25 (0.21-0.29)	0.21 (0.17-0.25)	0.26 (0.22-0.30)
Model 3	0.25 (0.21-0.30)	0.21 (0.17-0.25)	0.26 (0.22-0.31)
Model 4	0.16 (0.12-0.21)	0.12 (0.08-0.17)	0.16 (0.12-0.21)
36-37 weeks of gestation (n=1957)			
Model 1	0.23 (0.19-0.27)	0.20 (0.16-0.24)	0.25 (0.21-0.29)
Model 2	0.24 (0.19-0.28)	0.20 (0.16-0.24)	0.25 (0.21-0.30)
Model 3	0.24 (0.20-0.28)	0.20 (0.16-0.24)	0.26 (0.21-0.30)
Model 4	0.16 (0.11-0.20)	0.12 (0.08-0.17)	0.17 (0.12-0.21)
38-39 weeks of gestation (n=1669)			
Model 1	0.22 (0.18-0.27)	0.19 (0.14-0.23)	0.24 (0.19-0.28)
Model 2	0.23 (0.19-0.28)	0.18 (0.14-0.23)	0.24 (0.19-0.28)
Model 3	0.23 (0.19-0.28)	0.19 (0.14-0.23)	0.24 (0.20-0.29)
Model 4	0.15 (0.10-0.20)	0.11 (0.06-0.16)	0.15 (0.10-0.20)

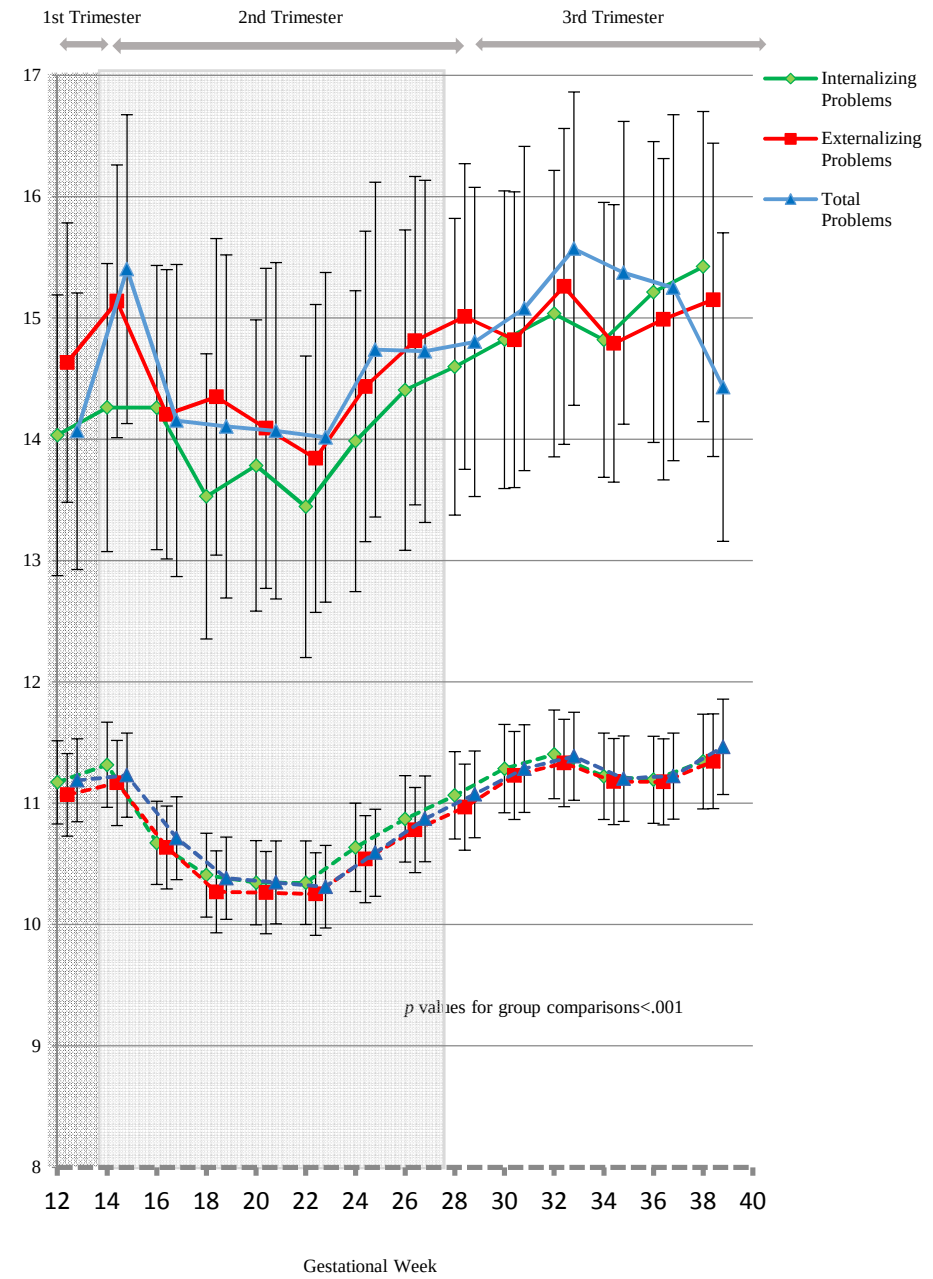
Note: Model 1 is adjusted for child's age and sex; Model 2 further for family structure, maternal age at delivery, parity, education, type 1 diabetes, chronic hypertension, history of depression before pregnancy, antidepressant and other psychotropic medication use, alcohol use and smoking during pregnancy, gestation length and child's birth weight adjusted for gestation length and sex: Model 3 further for pre-pregnancy obesity, hypertension-spectrum pregnancy disorders, and gestational diabetes, and Model 4 also for maternal depressive symptoms after pregnancy at the time of rating child's psychiatric problems. Bs and 95% CIs are unstandardized regression coefficients and their 95% CIs are from linear regression models. All independent and dependent variables are expressed in standard deviation units. All the associations are highly statistically significant ($p<.001$).

Table S4. Age-Specific Associations Between Trimester-Weighted Mean of Maternal Depressive Symptoms During Pregnancy and Child Psychiatric Problems

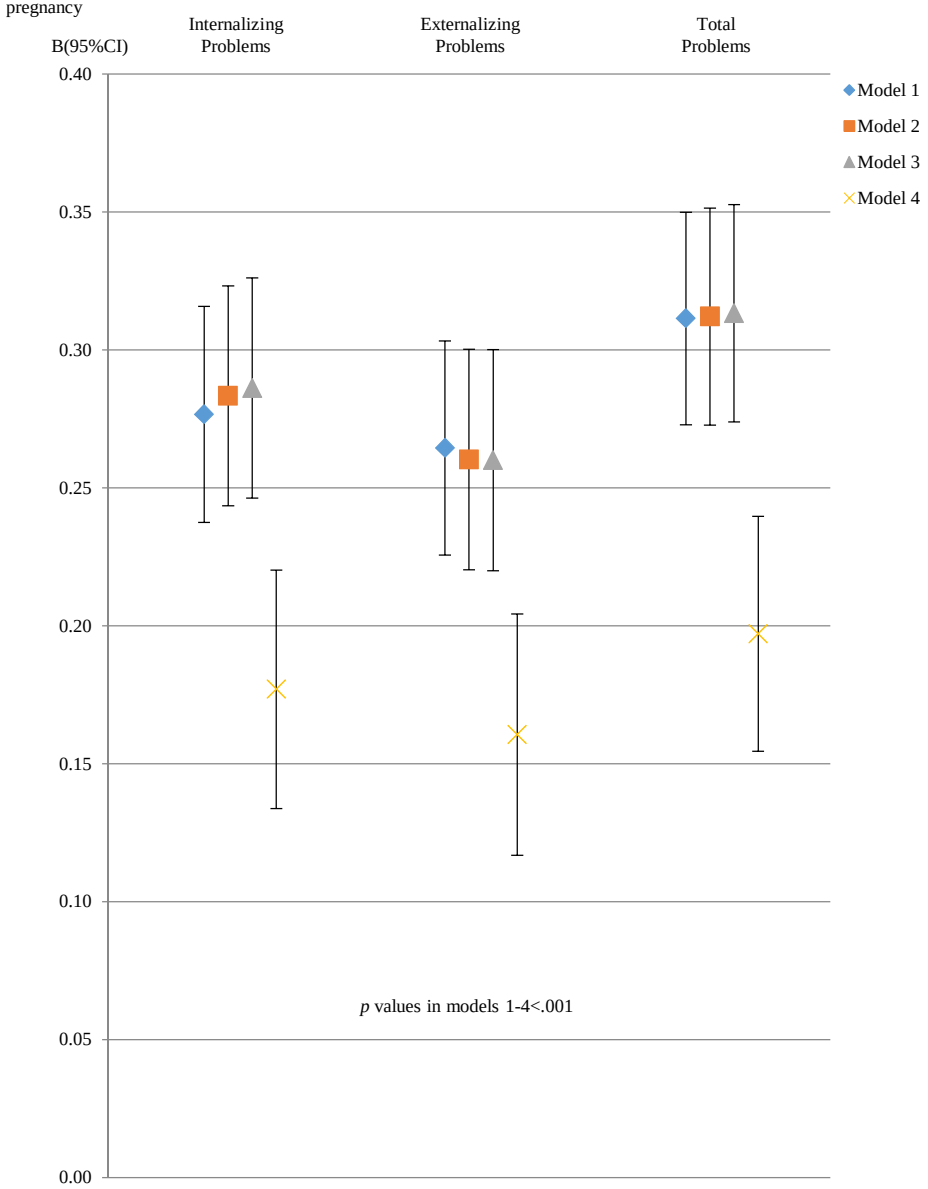
Age of the child	Model 1		Model 2		Model 3		Model 4	
1.9-3.9 years (n=1,564)	B(95 % CI)	p	B(95 % CI)	P	B(95 % CI)	p	B(95 % CI)	p
Internalizing Problems	0.29(0.25-0.34)	<.001	0.30(0.25-0.34)	<.001	0.30(0.25-0.34)	<.001	0.19(0.14-0.24)	<.001
Externalizing Problems	0.27(0.22-0.32)	<.001	0.27(0.22-0.31)	<.001	0.26(0.22-0.31)	<.001	0.17(0.12-0.22)	<.001
Total Problems	0.32(0.28-0.37)	<.001	0.32(0.27-0.37)	<.001	0.32(0.27-0.37)	<.001	0.21(0.16-0.26)	<.001
4-5.9 years (n=732)								
Internalizing Problems	0.25(0.18-0.32)	<.001	0.26(0.18-0.33)	<.001	0.26(0.19-0.34)	<.001	0.15(0.07-0.24)	<.001
Externalizing Problems	0.25(0.18-0.32)	<.001	0.25(0.18-0.32)	<.001	0.25(0.18-0.32)	<.001	0.15(0.06-0.23)	<.001
Total Problems	0.29(0.22-0.36)	<.001	0.29(0.22-0.36)	<.001	0.29(0.22-0.36)	<.001	0.17(0.09-0.25)	<.001

Note: Model 1 is adjusted for the age and sex of the child; Model 2 further for family structure, maternal age at delivery, parity, education level, type 1 diabetes, chronic hypertension, history of depression before pregnancy, antidepressant and other psychotropic medication use, alcohol use and smoking during pregnancy, gestation length and child's birth weight adjusted for gestation length and sex; Model 3 further for pre-pregnancy obesity, hypertension-spectrum pregnancy disorders and gestational diabetes; and Model 4 for maternal depressive symptoms after pregnancy at the time of rating the child's psychiatric problems. Bs and 95% CIs for main scales are unstandardized regression coefficients, and their 95% CIs are from linear regression analyses. Both the independent and dependent variables are expressed in standard deviation units.

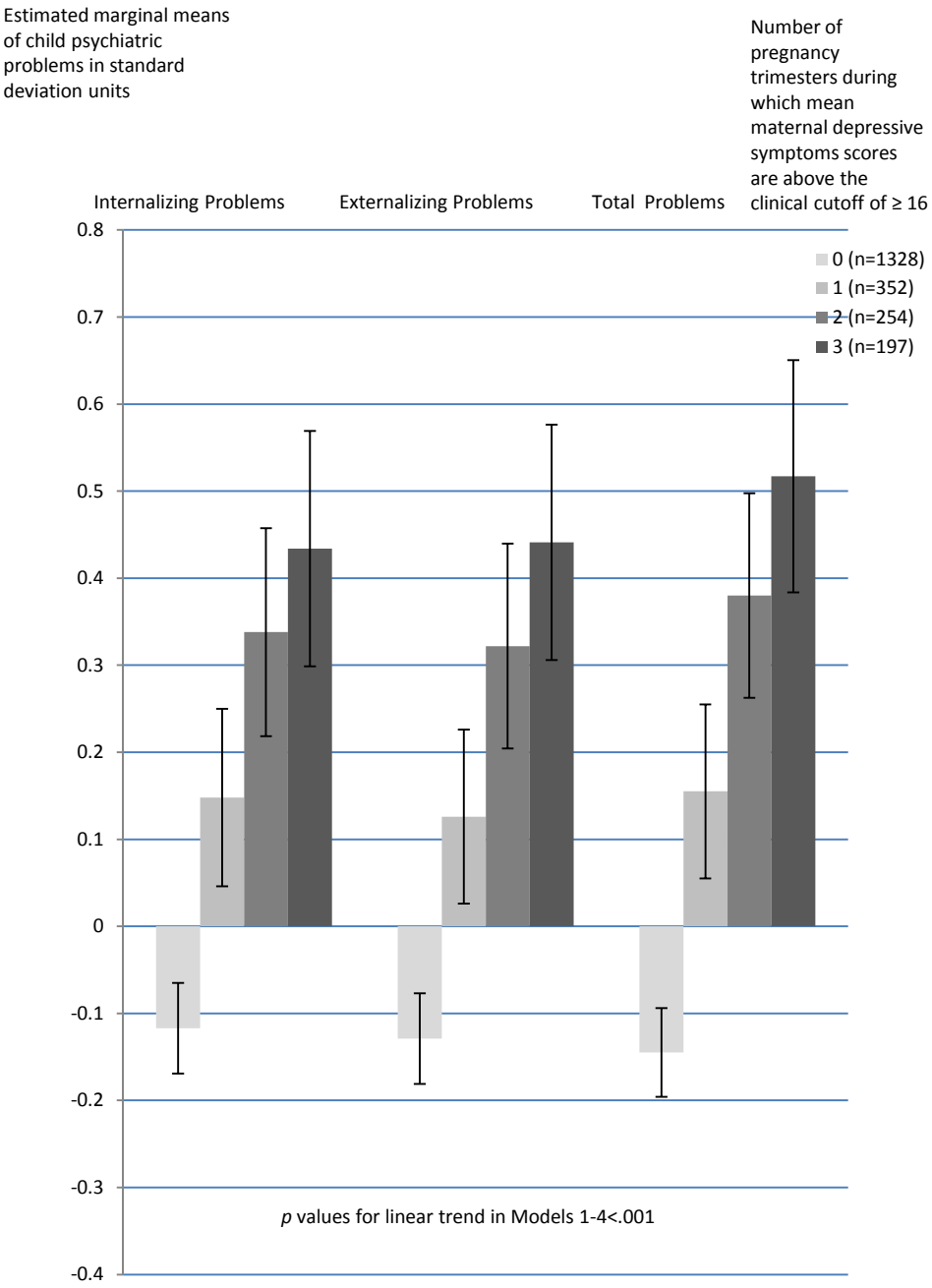
Panel A.



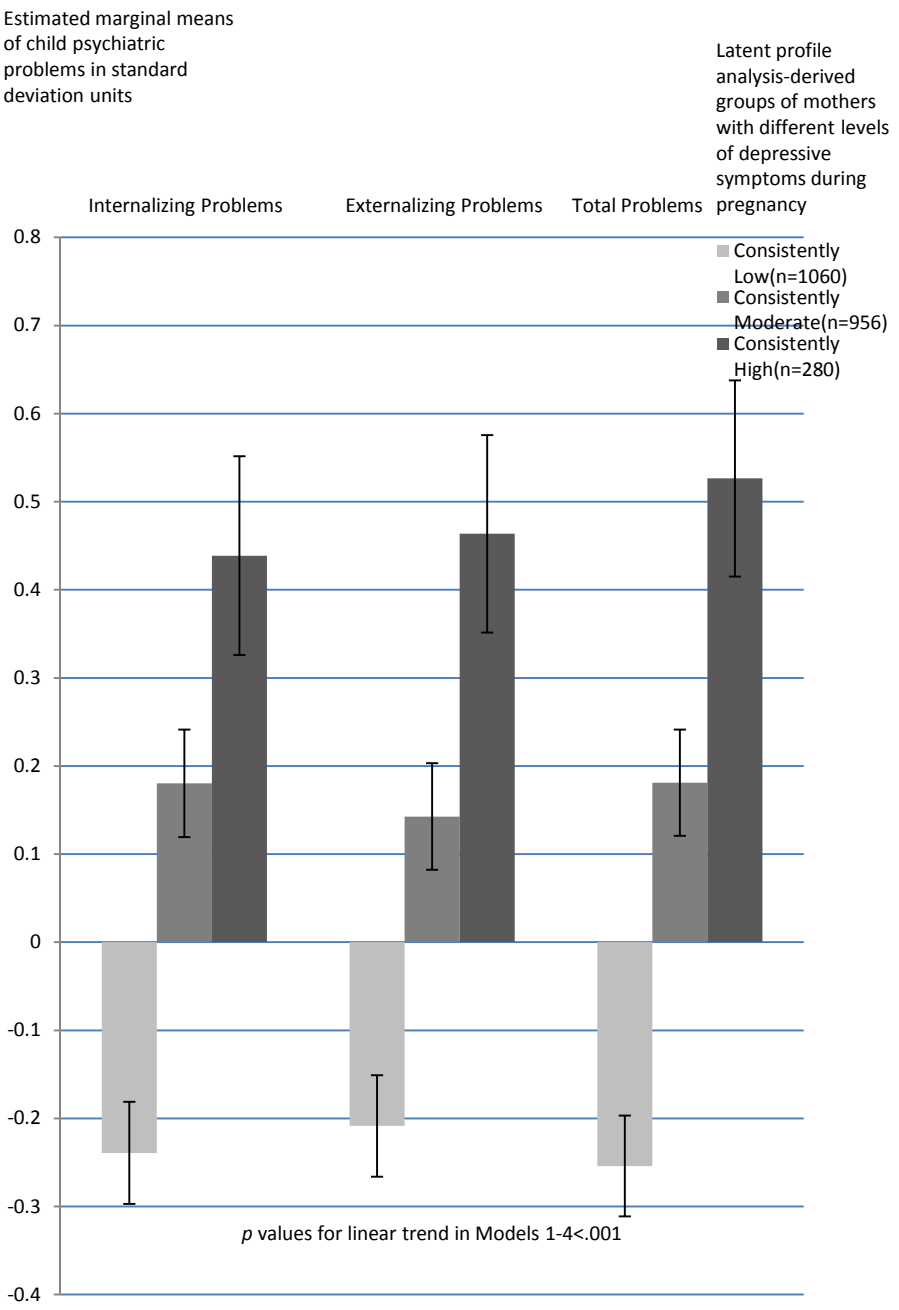
Panel B.



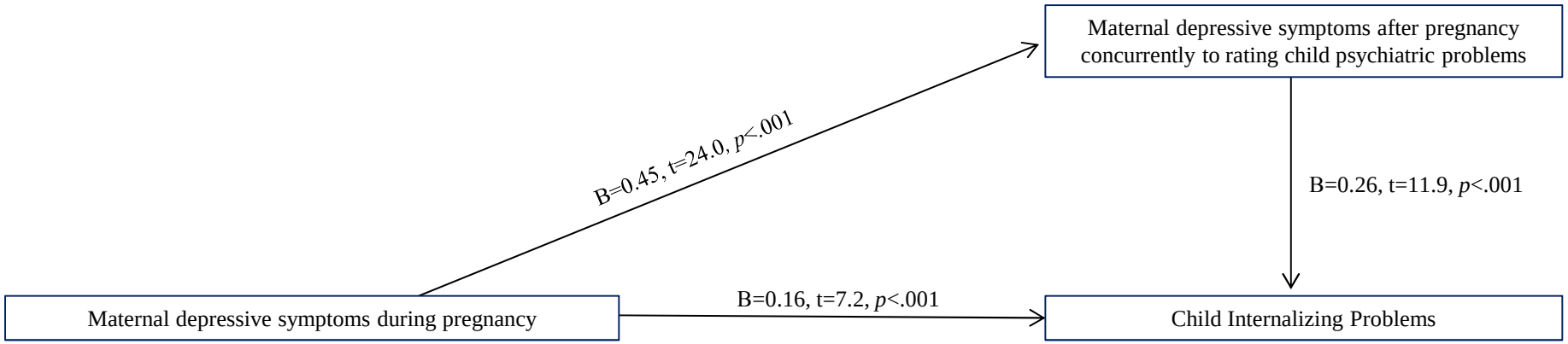
Panel A.



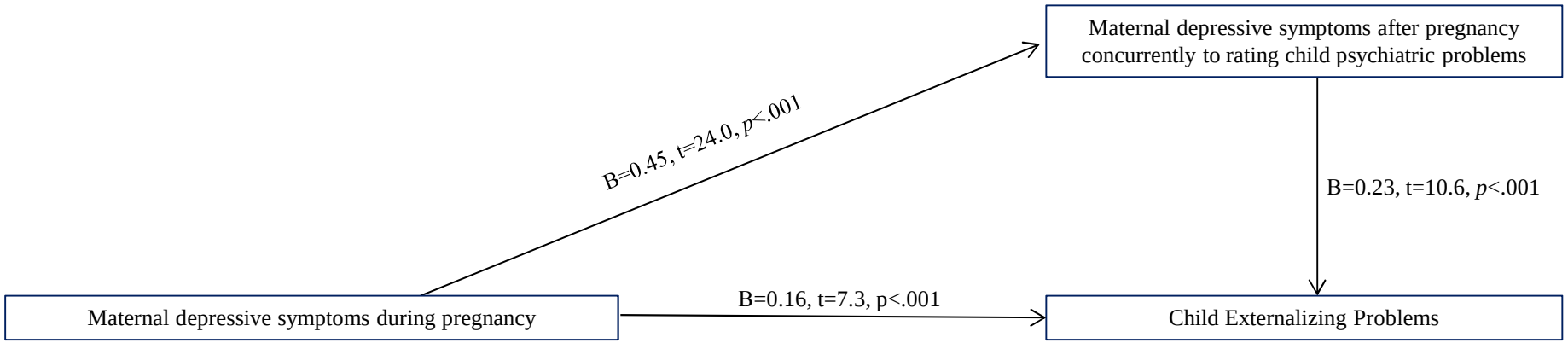
Panel B.



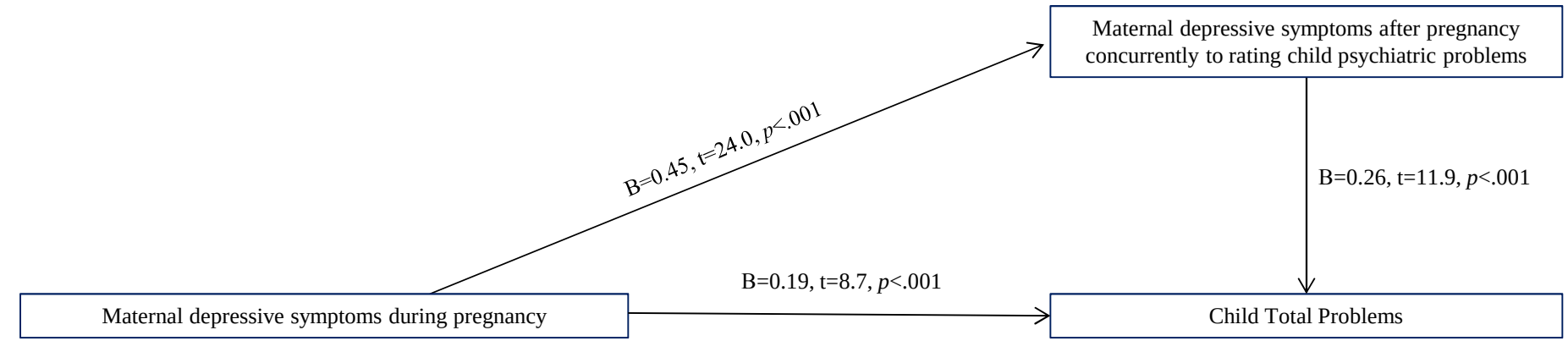
Panel A.



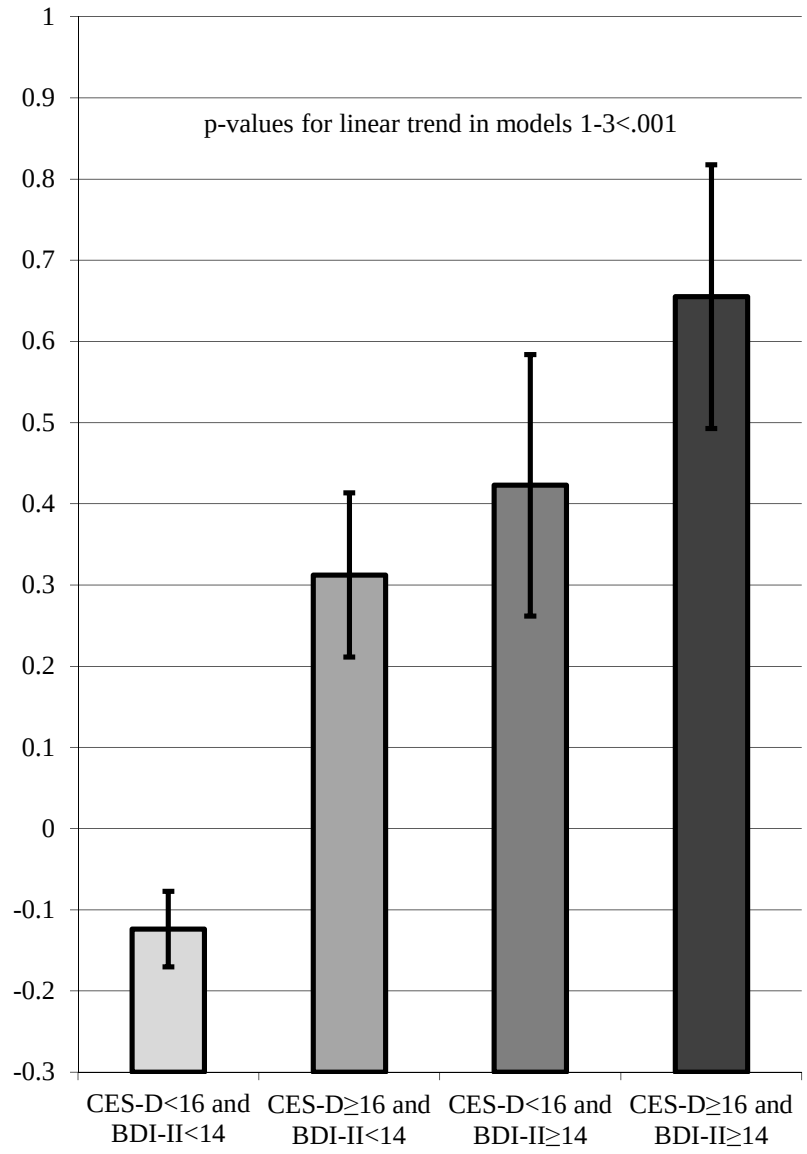
Panel B.



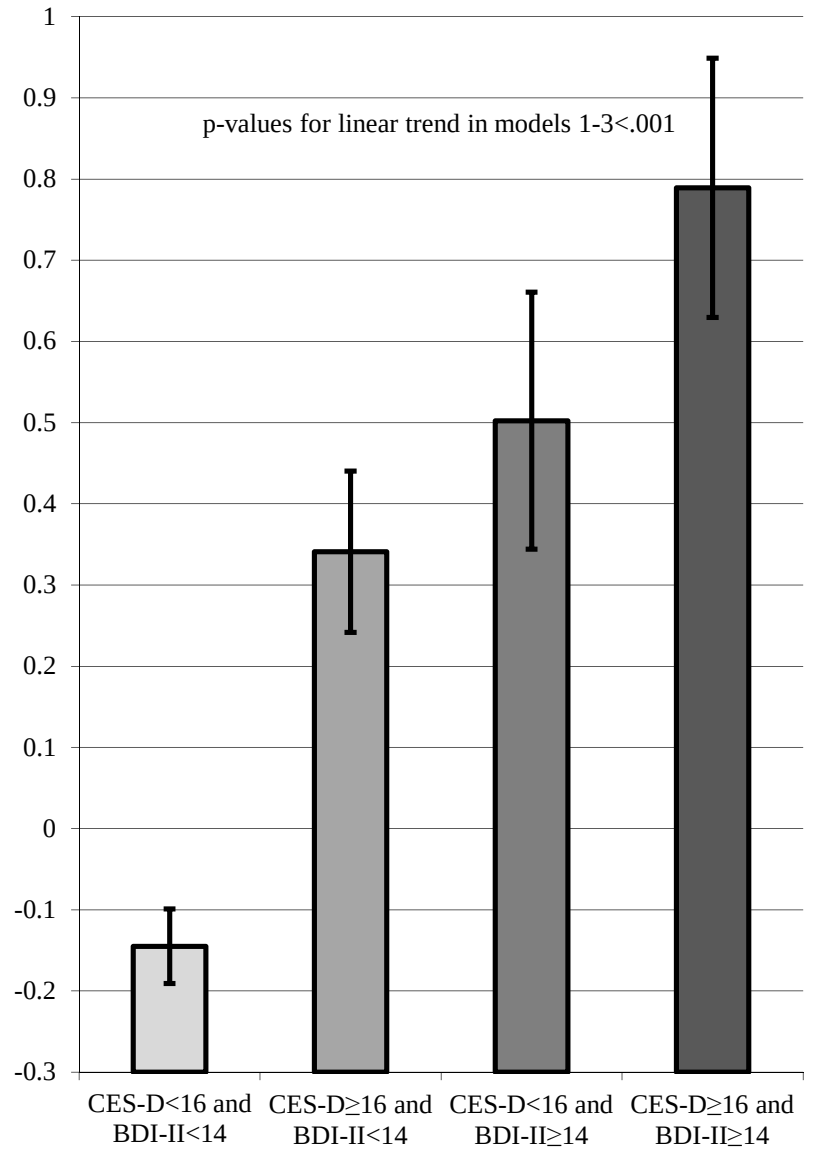
Panel C.

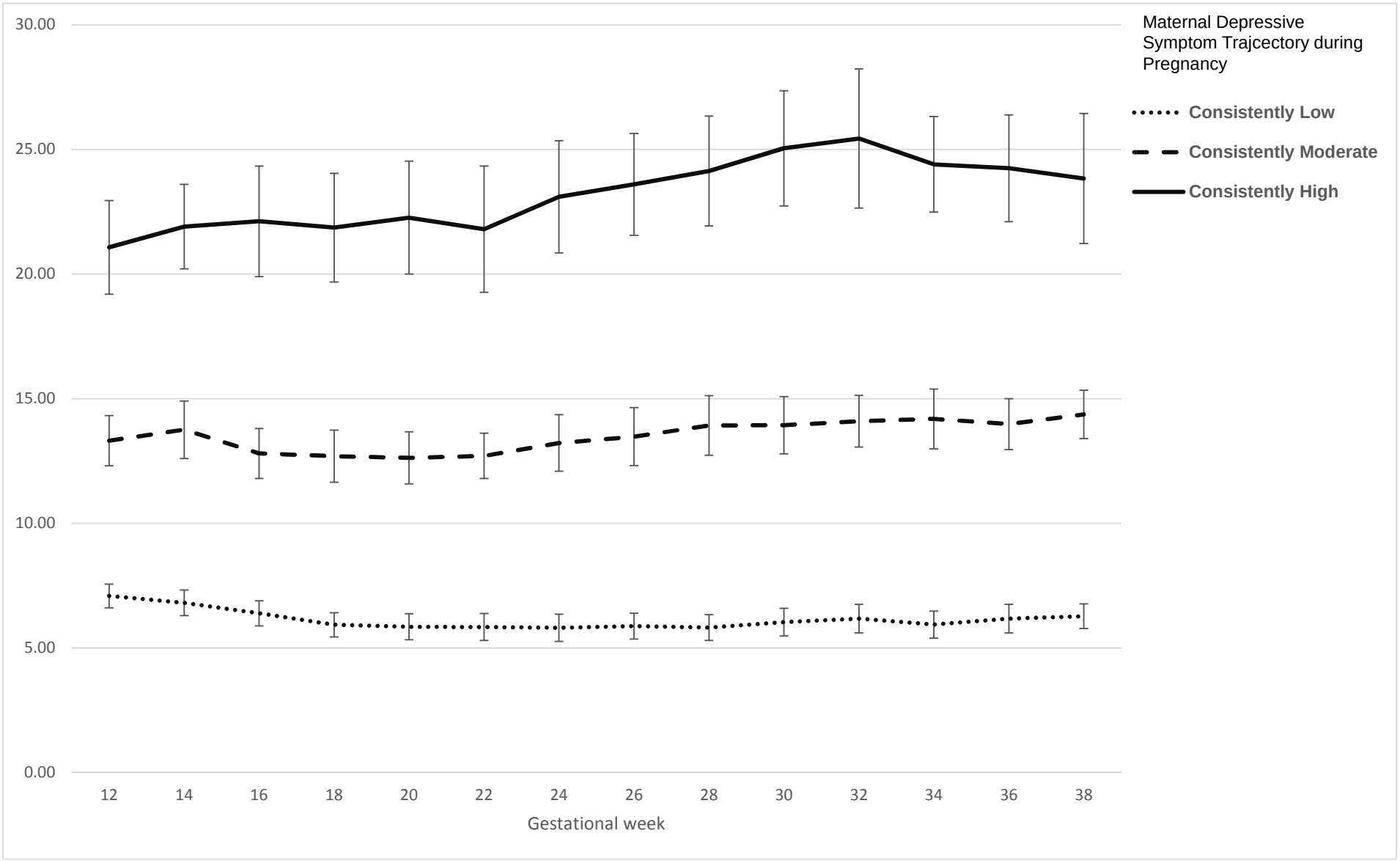


Panel A.



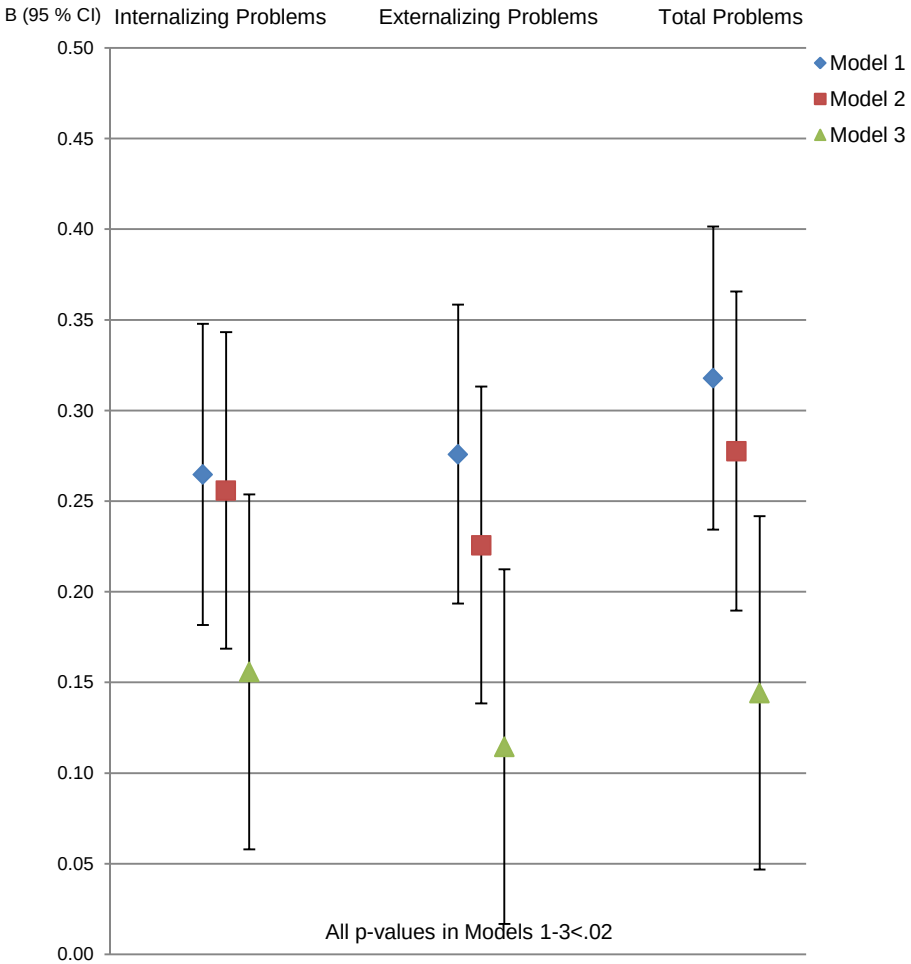
Panel B.





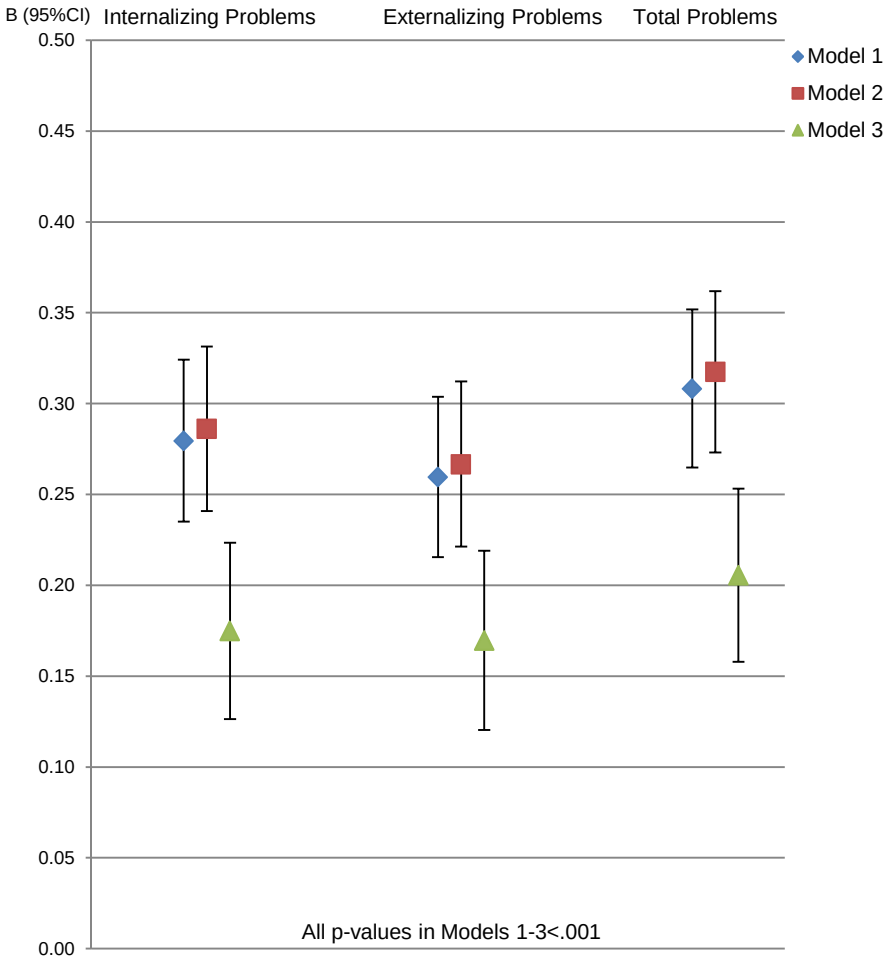
Panel A. With pregnancy Disorders

Standard deviation unit increase in child psychiatric problems per 1 standard deviation increase in maternal depressive symptoms during pregnancy



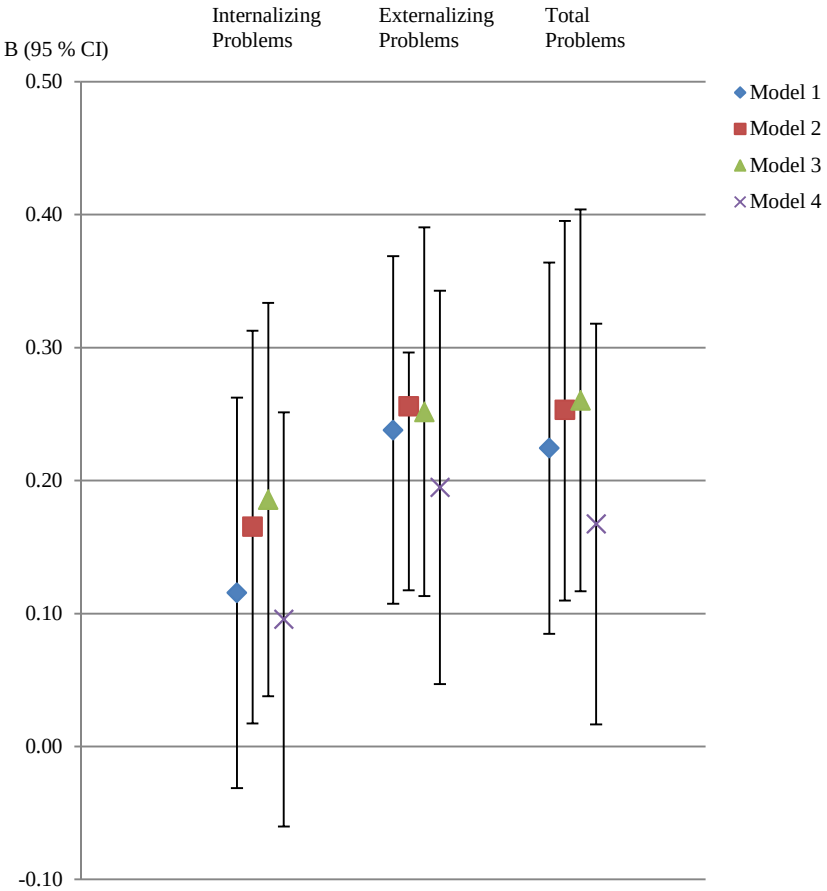
Panel B. Without pregnancy Disorders

Standard deviation unit increase in child psychiatric problems per 1 standard deviation increase in maternal depressive symptoms during pregnancy



Panel A. With History of Depression

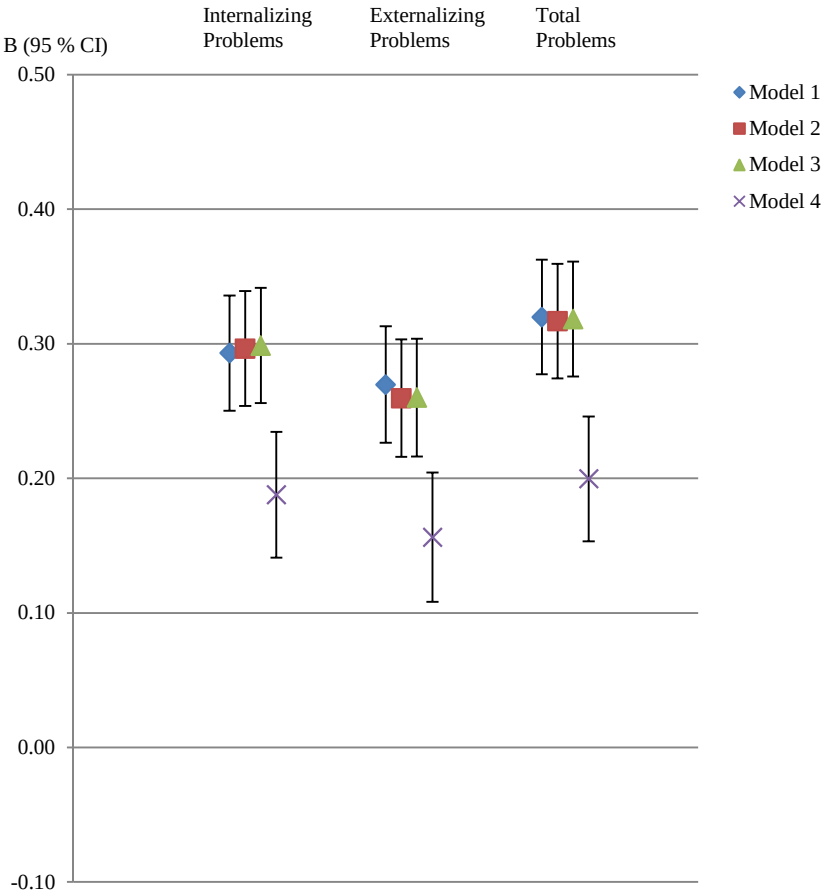
Standard deviation unit increase in child psychiatric problems per 1 standard deviation unit increase in maternal depressive symptoms during pregnancy



All p-values in models 1-4 for externalizing and total problems ≤.03, p-values for internalizing problems =.12, =.03, =.01., and =23 in models 1-4, respectively

Panel B. Without History of Depression

Standard deviation unit increase in child psychiatric problems per 1 standard deviation unit increase in maternal depressive symptoms during pregnancy



All p-values in models 1-4<.001